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## PACKAGING AND METHOD FOR SOLID DOSE ADMINISTRATION OF MEDICAMENTS

### FIELD OF THE INVENTION

This invention relates to inoculation of living animals, usually livestock or wildlife, with biologically active solid dose pellets. They may be administered subcutaneously as implants, or ballistically as a projectile.

### BACKGROUND OF THE INVENTION

Pellet implant systems which administer hormonal medicaments subcutaneously are known. Typically, they use a dosing gun to administer a series of pharmaceutical pellet implants, usually to the ear of an animal to provide sustained release of medicament. A dosing gun or implanter usually incorporates pellet magazines containing multiple doses of pharmaceutical pellets which are inserted subcutaneously into the ear tissue with an associated injection needle. The magazine channels are loaded with a series of identical pharmaceutical pellets for administration at the same injection site.

Implant technology, that is to say, procedures involving subcutaneous implants of pharmaceuticals and medical devices, are now well accepted and widespread in the areas of animal health and production enhancement. Growth stimulants are commonly used to enhance the body weight of animals which are raised for slaughtering, such as cattle, swine, sheep, turkeys, chickens and the like. A medicament in the pellet is normally formulated for continuous sustained absorption of the active ingredients over an extended period of time.

Solid dose ballistic projectiles shaped for penetrating the epidermal layer of living animal tissue are also known. These are typically fired remotely, using an airgun. They lodge totally within the tissues of the animal for later release of biologically-active medicaments into the animal tissue. They have an advantage over typical hand-held implant apparatus using a needle in that the inoculated animal need not be "captured".

This invention may be used with either type of solid dose administration, but has been found particularly useful with hand-held implant administration, more particularly where combined dosing of a plurality of biologically active materials is achieved with a single needle-inserted, subcutaneous implantation. For details of such implant systems, see my previous patent, U.S. Pat. No. 5,665,363, issued Sep. 9, 1997, and as well, other prior patents on pellet implant systems, such as U.S. Pat. No. 5,874,098, issued Feb. 23, 1999. Disclosures of each of these are incorporated herein by reference.

Particularly, when animals are multiply dosed, it is necessary for the medicament administrator to keep track of medicaments, and of which animals have in fact been dosed. This can be particularly bothersome when multiple dosing of a medicament occurs with a single subcutaneous implant, or shot, in the case of a ballistic implant. This invention has as its objective a new method, packaging and system for keeping track of and systematically administering a plurality of medicaments to animals so that the operator, or medicament administrator, can be confident that all desired medicaments have in fact been administered.

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### BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a front view of a bovine head, showing the ears.

FIG. 2 is a back view of a bovine head for illustrative purposes, showing the subcutaneous biological ear implant site.

FIG. 3 is a side view of a solid dosing implanter.

FIG. 4 shows a typical pellet magazine in perspective.

FIG. 5 shows a pellet magazine which is transparent, showing how the pellets are arranged in a prearranged multiple dosing order.

FIG. 6 shows how the prearranged dosing order for the pellets can be color-coded.

### SUMMARY OF THE INVENTION

A method and packaging for vaccinating or medicating an animal by implanting a solid dose medicament in an animal. The solid dose medicament, or plurality of such medicaments, are each color-coded to identify a particular active ingredient, then packaged in a pellet magazine through which the doses are visible, and thereafter the pellets are implanted, usually subcutaneously into the base of the ear or in the neck of an animal. The same system can be used for colored implants administered ballistically.

### DESCRIPTION OF THE PREFERRED EMBODIMENT

While the description here is given as a preferred embodiment of the invention, it is to be understood that the invention is not limited to preferred embodiment. Rather, the invention is limited only by the defining limits of the claims, as opposed to any statements in the specification relating to the preferred embodiment.

A calf 10 is indicated for illustrative purposes of showing the working of the medicament implant system. A suitable solid dosing implanter 12 of known construction can be used. Such devices generally include a housing 14 with a pistol grip 16, a trigger 18, and a subcutaneous implant needle. The pellet implant magazine 22 is inserted into the implanter apparatus 12, and moves downwardly there-through as trigger 18 is pulled, unloading its biological or pharmaceutical dose through a needle as trigger 18 is pulled. This action forces the multiple doses through the bore of the needle (not depicted) attached to the implant apparatus 12, and into a subcutaneous puncture, particularly in the base of the ear 24 as illustrated at 26, FIG. 2, or in the neck. For details of such a method, see my earlier U.S. Pat. No. 5,665,363.

Pellet magazine 22 is illustrated in perspective in FIG. 4 and in FIG. 3 as it would enter from the top and exit below the implanter apparatus 12. It can be seen that pellet magazine is made of an inert, see-through polymeric plastic material. The magazine 22 used with implanter 12 typically contains multiple, parallel-aligned, pellet dosing columns or chambers 28. As illustrated, the chambers are generally of such a construction that each has a hollow internal core. The chambers 28 are in side-by-side parallel relation, as illustrated.

Each chamber 28 is loaded with a plurality of discrete dosing pellets in columnar relationship, as illustrated in FIG. 5 at 30. Individual pellets in similar stacked relationship are shown in FIG. 6. The individual pellets 32 are composed of an identified biologically active ingredient in conjunction with one or more excipients formed as part of a polymeric base release system such as described in my earlier U.S. Pat.

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No. 5,665,363. Each of the solid dose pellets 32 include a wide range of biologically active medicaments. Indeed, the particular medicament used for pellet 32 is not a limitation on the invention. For example, the medicaments may be hormones, minerals, vitamins, antibiotics, antigens, antibodies, tranquilizers, dewormers, etc.

Preferably, the biologically active pellet comprises about 2% to 70% by weight of a medicament. More preferably, the biologically active pellet comprises about 3% to 50% by weight of the medicament, most preferably about 4% to 20% by weight.

Typically, the dried powder mixture is blended with a lubricant and pelletized into final form. Lubricants facilitate the release of the pellets from the pelleting dies.

A list of lubricants that can be used in the practice of the invention includes, but should not be limited to, magnesium stearate, calcium stearate, sodium stearyl fumarate, stearic acid, sodium lauryl sulfonate, polyoxyethylene (carbowaxes), polyethylene glycols, glycerol behenate, hydrogenated vegetable oils and mixtures thereof. Preferably, the lubricant contains calcium stearate.

Generally, the biologically active pellet comprises an effective pellet-forming amount of a lubricant. Preferably, the biologically active pellet comprises about 0.2% to 5% by weight of a lubricant. More preferably, the biologically active pellet comprises about 0.5% to 3.5% by weight of a lubricant, most preferably about 1.0% to 2% by weight.

TABLE 1

	% By Weight of the Biologically Active Pellet		
	Working Range	Preferred Range	Most Preferred Range
Biologically Active Material	2%–70%	3%–50%	4%–20%
Excipients	balance	balance	balance
Lubricant	0.2%–5%	0.5%–3.5%	1%–2%

Optionally, the biologically active pellet can comprise additional excipients. These additional excipients can be added to the biologically active pellet to provide increased strength, to control dissolution rates, to improve powder handling, e.g., flow and the like, or to improve the efficacy of the product. A list of additional excipients that can be used as the biologically active pellet of the invention includes, but should not be limited to: precipitated or fumed silicas, sodium starch glycolates, calcium phosphate, calcium carbonate, dextrans, polyvinyl pyrrolidone, hydroxypropylcellulose, hydroxypropylmethylcellulose, polylactic acid, polyglycolic acid, magnesium aluminum silicates, microcrystalline cellulose, sodium carboxymethylcellulose and mixtures thereof. Preferably, these additional excipients are less than about 50% by weight of the biologically active pellet. More preferably, these additional excipients constitute less than about 40% by weight of the biologically active pellet, most preferably 25% by weight.

Pellets may be generally prepared as follows:

A liquid suspension containing, for example, bacterial cells and associated products adsorbed on aluminum hydroxide gel is mixed with sufficient mannitol to yield a final weight of 15 milligrams per dose of product. The suspension is dispensed into containers, frozen, and the water removed under vacuum. After freeze drying is complete, the dried powder is harvested. The powder is processed to reduce the particle size to less than 0.1

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millimeter, and sufficient calcium stearate (approximately 1% by weight) is added for lubrication.

The powder blend is then tableted on a conventional tableting machine to produce uniform pellets. A typical formulation for the above pellets would be:

Freeze-dried powder	15
Calcium stearate	2
Precipitated silica	0.5
Filler,	balance

(Powder has 10 parts bacterial antigen and 5 parts mannitol)

Pellets produced as above may, if desired, be converted to delayed release pellets by coating with materials that will delay the escape of the medicament to the body. Materials that are useful for this are compounds that will slowly degrade or dissolve in the body fluids. Examples of materials suitable for use are hydrolytically unstable polymers such as polylactic acid, polymers such as ethylvinyl acetate that are slow to dissolve in body fluids, or waxy solids, such as cholesterol, that have a limited solubility in aqueous fluids. These materials can be applied to the tablet as coatings and will act to delay the release of the active ingredient from the pellet.

There are a number of coating techniques available for adding the delayed release coatings to the pellets. Rotating drum coaters or fluidized bed coating processes can be used. Any process that can apply a uniform coating in a controlled manner can be used. The thickness of the coating and water solubility will determine the delay before the product is released.

The biologically active pellets of the invention can be formed into any possible shape that the pelletizing machine is capable of making. Preferably, the shape and size of the biologically active pellet is one suitable for implanting into the animal. More preferably, the shape of the biologically active pellet is such that it can be used in conjunction with an implant gun. Most preferably, the shape and size of the pellet is adapted for implanting the biologically active pellet subcutaneously into an ear or neck of the animal.

In general, the size of the biologically active pellet depends on the dose to be administered to the animal and compatibility with the implant gun and needle used.

The biologically active pellets of the invention can be implanted into any animal which is capable of responding to the biologically active material. Generally, these animals include, but should not be limited to, cattle, hogs, horses, cats, dogs, sheep, goats, for example. In a preferred embodiment of the invention, the animal is domestic cattle.

The biologically active pellet can be subcutaneously implanted into any area of the animal which allows the biologically active pellet to come into contact with tissue fluids. Preferably, the biologically active pellet is implanted into an area of the animal which minimizes or eliminates lasting damage to edible tissue of the animal. More preferably, the biologically active pellet is implanted into an ear, the neck, the tail-head or flank areas of the animal, thereby reducing potential damage to edible tissue. Most preferably, the biologically active pellet is implanted into the ear of cattle, thereby eliminating damage to edible tissue.

In our earlier patent, I found that implanting the biologically active pellet into an ear of the animal does not result in an undesirable "drooped ear", or "down ear" in the animal. As with any product administered through the skin, sanitary methods must be followed to reduce the likelihood